

## ① Definition of pharmacology :

drugs

study

It's the science that deals with the study of drugs and their effect on living systems (treatment, prevention, diagnosis, amelioration (تحسين) of diseases)

## ② History of Pharmacology :

بعضها يا جماعة من الجزء ده من مواد اجتماعية وليس له أي أدنى أهمية من بس لازم برفقه نقرأه من الكتاب وإحنا هكتب أهم علماء علمه يمكن نتسأل فيهم.

\* 1<sup>st</sup> we have the honour that ancient Egyptians were the first to know about this field.

### بردية إبير : Ebers papyrus

- Written in Egypt in 16<sup>th</sup> century B.C. (Before Christ)
- described products comes from animals as lizards (السمكالي), blood, swine (خنزير بري) teeth, goose (الأوز) grease together with some plant's extract.

overtime new approaches got some plant extracts having obvious pharmacological effect



- ① Poppy  $\rightarrow$  opium  $\rightarrow$  morphine  $\rightarrow$  analgesic
- ② Cinchona  $\rightarrow$  extract  $\rightarrow$  antimicrobial drug.

### Materia medica

\* a Science developed to understand origin, preparation, therapeutic application, of medicinal comp.

\* it said that every disease has a cause for which there's a specific drug (remedy)

\* The drug administration is based on testing dose-response relationship

In 1897

Felix Hoffman developed aspirin (analgesic).

In 1971

Sir John Vane discovered mode of action (MOA) of aspirin.

In 1908

Paul Ehrlich described drug-receptor binding by a very famous & important sentence saying

"Agents do not act unless they are bound"

وَكَيْفَ نَبْقَى خَلْقَنَا الْمَوَادَّ الْإِجْتِمَاعِيَّةَ وَنَبْقَى نَحْنُ فِي الْمَعْمُورِ

رَكَنُوا أَرْجُو كُمْ



### ③ Division of Pharmacology :

#### Pharmacodynamics

Effect of 1 Drug on 1 body

\* What the drug does to the body

\* It studies the Biochemical & Physiological effects of drugs & their MOA (mode of action).

\* It studies :

① Drug-receptor interactions  
ie// Binding, dose-response, effect

② Signal transduction

③ MOA pathways

④ Adverse effects.

أهم حاجة إنك تعرفوها بتعرفنا تأثير الدواء على الجسم

#### Pharmacokinetics

\* What the body does to the drug.

\* It studies :

① absorption

② Distribution

③ Metabolism

④ Elimination

أهم حاجة إنك تعرفوها  
بتعرفنا تأثير الجسم  
وتعامله مع الدواء

بتقدر تغيرها على  
ال pharmacodynamics

#### Pharmacogenetics

\* Unusual responses to the drug caused by genetic differences between individuals

\* example :

① allergies

② unusual side effects

③ unusual toxic effects.

\* يعني واحد آخذ دواء معين  
وآعطى مفعوله عادي جداً

وواحد تاني آخذ الدواء  
وآعطى مفعوله لكنه بسبب له  
حساسية وطفح جلدي شديد

هذا بسبب genetic differences  
وهذا ما تدرسه ال Pharmacogenetics



#### ④ Definition of drug :

- \* They are chemical substances (agents) that uniquely interact with specific target molecules (receptors) in the body  $\rightarrow$  thereby producing a Biological effect
- \* They can be stimulatory or, inhibitory.
- \* They affect living processes
- \* They are used in treatment, prevention, diagnosis or, amelioration (تخفيف) of diseases

#### ⑤ Drugs Produce their effects virtue (بواسطة)

- ① Acidic or, Basic properties eg: antacids
- ② Surfactant properties eg: Amphotericin B
- ③ Ability to denature proteins eg: Astringent
- ④ Osmotic properties eg: Laxatives & diuretics
- ⑤ Physicochemical interactions with membrane lipids  
eg: general & local anaesthetics



دلو قتی هتکلم عن Topic جديد وحوار ولازم يتفهم بكل ما فيه

# Receptors

- \* Most drugs combine  $\epsilon$  specific receptors to produce a particular response
- \* This association or binding take place by precise physiological & sterile interaction between specific groups of the drug & the receptor.

Protein in body may be in form of  
أي بروتين في الجسم قد يكون في شكل

Carrier or Receptor or enzyme

has 2 main types

Membrane bound receptors

يوجد receptor موجودة في الخارج على سطح  
ال cell على ال membrane

Intracellular & nuclear receptors

يوجد recept. موجودة داخل ال cell  
أو في ال nucleus

has 3 types :

examples :

- ① G protein linked receptors as muscarinic, noradrenergic, dopaminergic
- ② Enzyme linked as Tyrosine kinase
- ③ Ligand gated channels as Nicotinic, GABA, Glutamate

- ① hormone receptors.
- ② Autacoid eg histamine
- ③ Growth factors
- ④ Insuline



Drug interact and bind  
Receptor by specific  
gp.

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Drug-receptors interaction:

after binding signal  
Appear Then Amplified  
and produce effect

هنا شرح بالعربي الأول وبعضهم نقول الكلمتين اللغة.

السواء يوصل في ال receptor هذا يؤدي إلى ظهور signal  
ال signal ده بتعمل بعض ال events أو cellular activities  
التي تعرف إلى تضخيم ال signal.  
لما ال signal تضخم ال response ال إحنا عايزين منه  
ال drug يظهر (effect).

\*) It serves as a signal to trigger cascade (فيضانه)  
of events (collection of cellular responses)

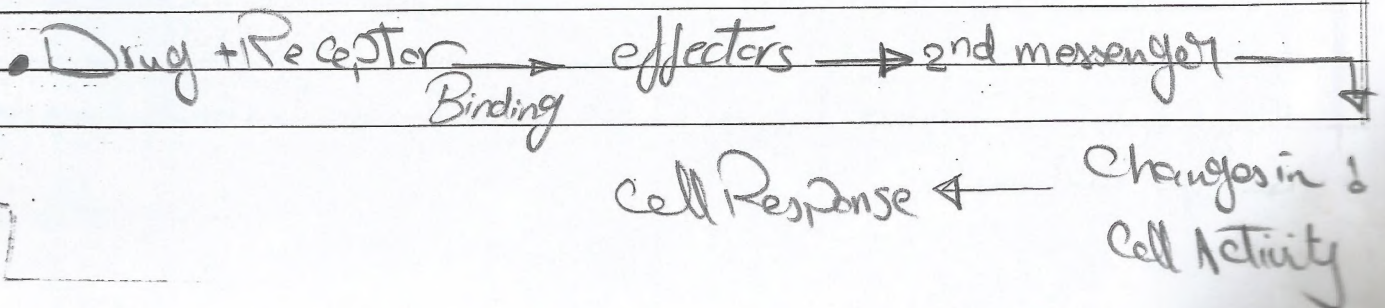
\*) These events serve to amplify the signal & Produce  
effect.

طيب إيه هي ال events ده يا عم أنت؟

\*) لما السواء يوصل في ال receptor هناك بعض الموارد بتطلع تسمى  
effectors وهذه ال effectors بتتسبب في ظهور بعض  
الموارد الأخرى تسمى 2<sup>nd</sup> messenger التي تتسبب تغيرات في  
ال cell activity و ظهور ال cell response للسواء المعطى

Effectors:

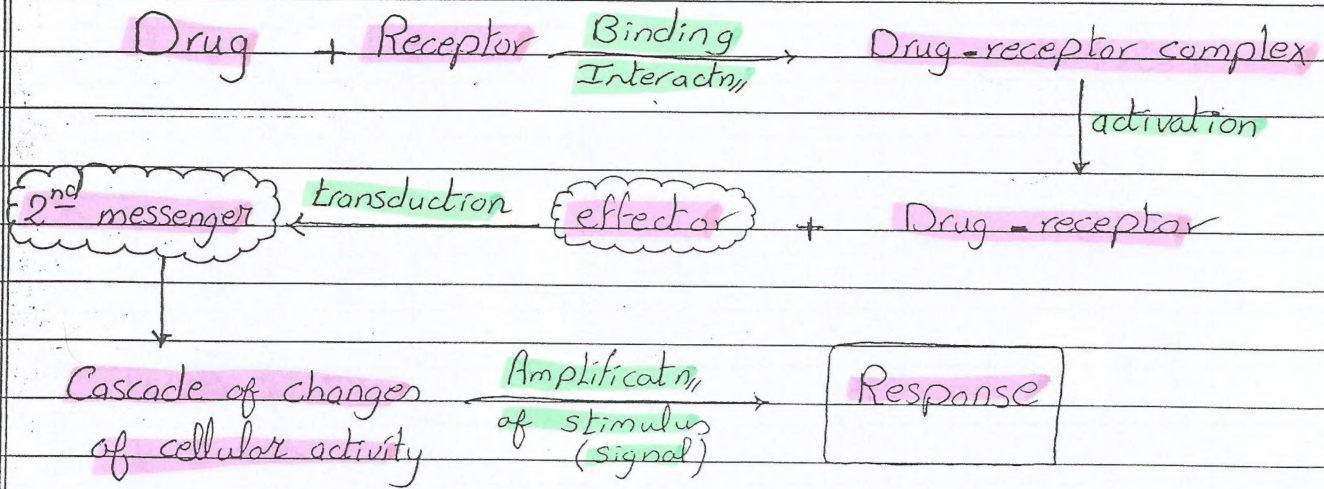
"they are molecules which translate  
the drug-receptor interactions into changes  
in cellular activity"





N.B effector  $\rightarrow$  converts (binding of Drug to Receptor) to stimulus

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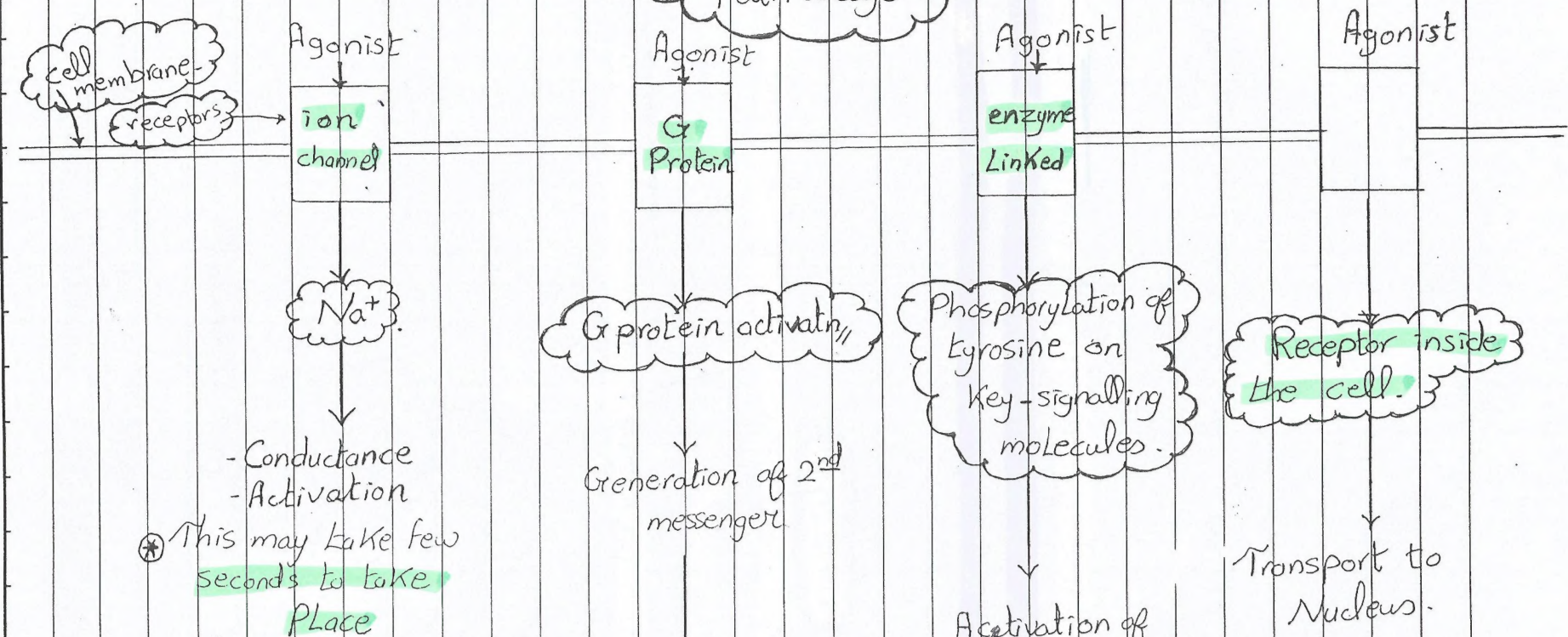
& Here are Some effectors  
& their corresponding 2<sup>nd</sup> messengers

Effector	2 <sup>nd</sup> messenger.
Adenylate cyclase (AC)	CAMP
Guadenyl cyclase (GC)	CGMP
Phospholipase A <sub>2</sub> (PLA <sub>2</sub> )	Arachidonic acid
Phospholipase C (PLC)	DAG $\rightarrow$ diacyl glycerol IP <sub>3</sub> $\rightarrow$ inositol triphosphate
Nitric oxide synthase	Nitric oxide (NO)
Ions channels	Na <sup>+</sup> , K <sup>+</sup> , Ca <sup>2+</sup>

الذكورة لم تهتم بال example أوى من يمكن هنا خذها تاني به كذا على العموماً هنا  
هنا أكرها طبعاً



& Here's a helping sketch to show Receptor Signalling Pathways



Q How G-protein make Amplification for 1 signals ??

Normally Receptor bind  $\bar{e}$  Adenyl cyclase (which converts  $\text{ATP} \rightarrow \text{AMP}$ )

- Receptor bind  $\bar{e}$  G-protein and G-protein bind  $\bar{e}$  20 Adenyl cyclase.

\* This may take a longer time (few minutes)

\* It takes few hours to appear its effect.

\* This takes some days to appear its effect



\* طبيب احنا كده عرفنا تأثير كل molecule مع ال Drug على كل molecule مع ال receptors

\* دالوقتى باينزيم نعرف تأثير كيمياء الدواء وده يرضك بيع ال

Drug - Receptor interactions :

① Theory & assumptions

1-) drug - receptor interactions follows mass action Relationship

2-) This means that only one molecule of drug occupies one receptor reversibly

3-) Magnitude of response of cell is proportional to total receptor sites occupied by drug molecules.  
why??  
oo Response to drug is graded [Dose dependant]

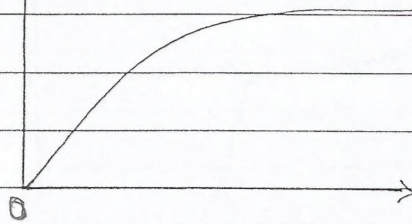
دوال استجابه الكلام ده ال Dose Response Curves



# Dose - Effect (conc. response) Curve

## hyperbolic curve

E  
(effect)



↑ Dose → ↑ Binding between Drug + Receptor → ↑ Drug-Receptor Complexes → ↑ effect Till

L (Ligand = binding)

D (Dose)

C (conc.)

all Receptors occupied  
→ Drug after this  
any ↑ in Drug Dose  
not lead to any

(\*) at zero conc. → no effect at all change in response  
∴ we start from the origin

(\*) by increasing conc (dose) → more drug molecules bind to receptors giving more drug-receptor complexes producing increasing effect

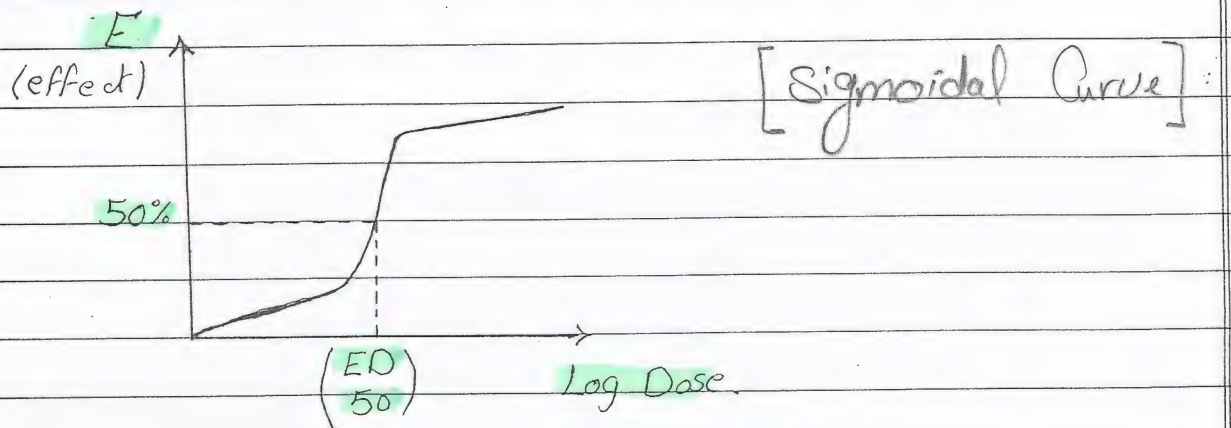
hyperbolic

(\*) this will increase gradually till all receptor molecules are occupied by drug molecules giving the maximum effect

(\*) after this Point → the increase in drug conc. won't affect the response as all receptor molecules are already occupied.



By taking Log to Dose  
to change the hyperbolic  
Curve to a Sigmoidal  
Curve



(\*) We carried out log Dose  $\rightarrow$  to get this curve that will help us alot in getting (ED 50)

What's (ED 50)?

It's the Dose that gives 50% of the Effect of the drug.



(\*) دلو قتي هنتقل لبعض ال Expressions الهامة جداً  
واللي لازم تكون عارفها وفاهمها و حافظها ع ظهر قلب  
ولازم تعرف الفرق بينهم

(\*) **Affinity** :

It's the ability or tendency of  
an agonist to bind to its receptor  
to form a complex.

يعني ال agonist (drug) اللي عندي ده هل له قابلية أو  
نفس إنه يصلح في ال receptor ولا لا

(\*) **Potency** :

It's a measure of how much  
drug is required to elicit (produce)  
a certain response

يعني أنا دلو قتي عندي في الصيدلية دوائين المقروض انهم  
بيعطوا نفس التأثير لكن واحد منهم لازم آخذ 100mg  
والثاني ممكن آخذ منه 25mg فقط ليعطي نفس التأثير

هو يبقى الدواء الثاني (25mg) is more potent  
و الدواء الأول (100mg) is less potent

- what is meaning of Drug A more potent Drug B?

This mean that 1 Drug A give Same Act  
+ Response of 1 Drug B but by using less

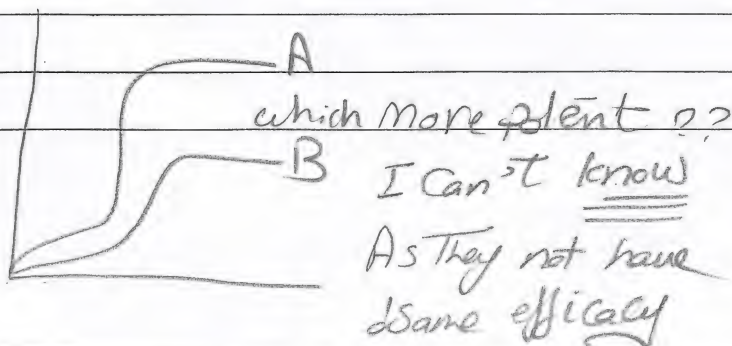
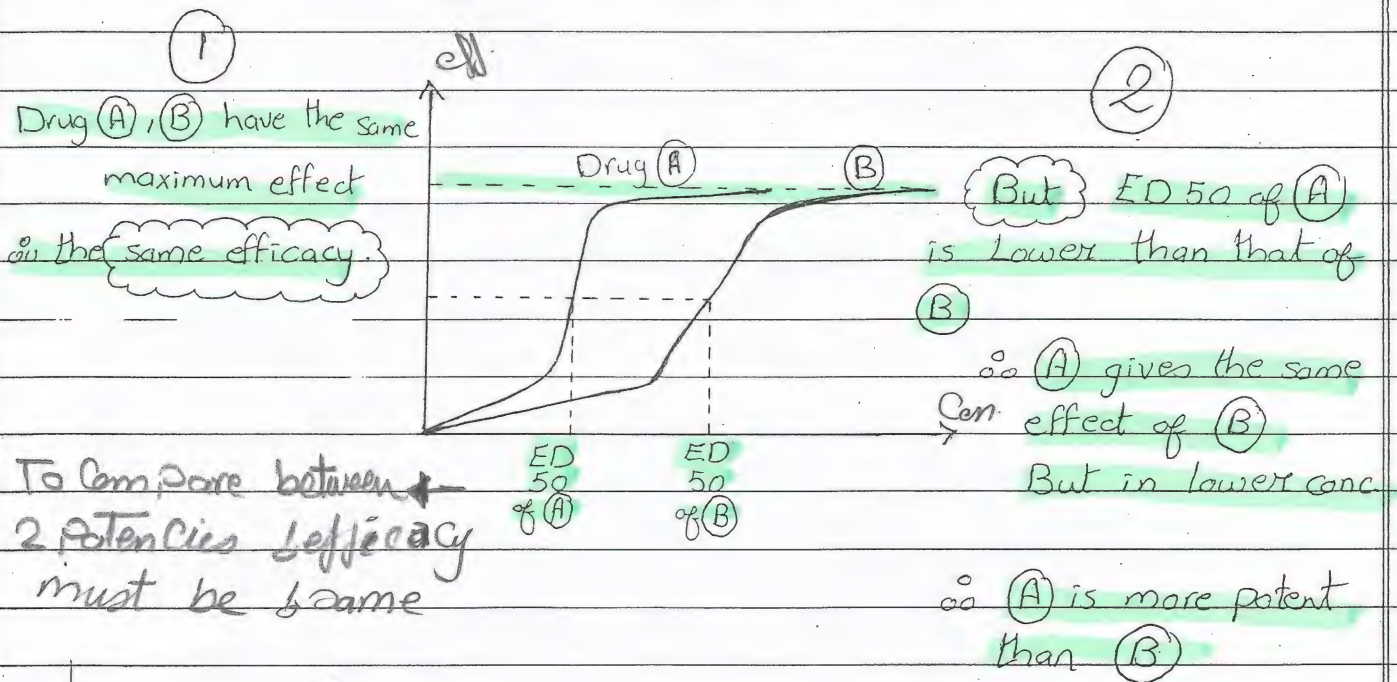


## Efficacy (intrinsic activity):

Drugs which can give maximum response  
(maximum effect of drug)

- if we have 2 drugs
- they occupy the same no. of receptors
- But one of them gives a greater biological response than the other
- then that drug (gives ↑ response) has higher efficacy

## Potency & Efficacy Relationship





و تعالوا نستوفى برضه ما يبقى ال Expressions الله جده  
جده جده

## AGONIST

### \* Full Agonist :

It's the drug which :

- ① has affinity to receptor
- ② has intrinsic activity (efficacy)

### \* Partial agonist :

It's the drug which :

- ① has affinity to receptor
- ② has some intrinsic activity (efficacy)

∴ it binds to receptor but never  
Produces maximum effect

∴ used only in mild cases but  
severe cases requires full agonist




① has affinity to the receptor

② has zero intrinsic activity (efficacy)

ie, no response is ever achieved by its binding.

يعني حاجة من خيطة كده من جانت ووصلت في الـ receptor  
ولم تفعل شيئاً.

receptor. ۱۱ Blocker  ؟

## Types of antagonism :

(1) Pharmacological

⊗ Competitive

→ binds with the receptor without activating it.

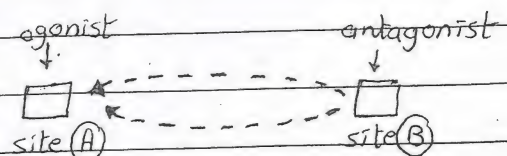
→ Prevent binding of agonist

→ as atropine to acetylcholine

By  $\uparrow$  dose of agonist we can get rid of antagonist & vice versa.

(\*) Non competitive

→ Binds to different site than agonist exerting its antagonistic action via the other binding site



site (B) affects (A) stopping action of agonist.



## ② Chemical

inactivating the agonist chemically  
example :

Dimercapol (antagonist) Being used to treat  
arsenic poisoning (agonist)

## ③ Pharmacokinetic

alters the way ~~by~~ which the body deals with  
the drug ~~ex~~ phenobarbital  $\uparrow$  metabolism of warfarine  
 $\Rightarrow$  ~~so~~ anti coagulant Activity

## ④ Physiologic

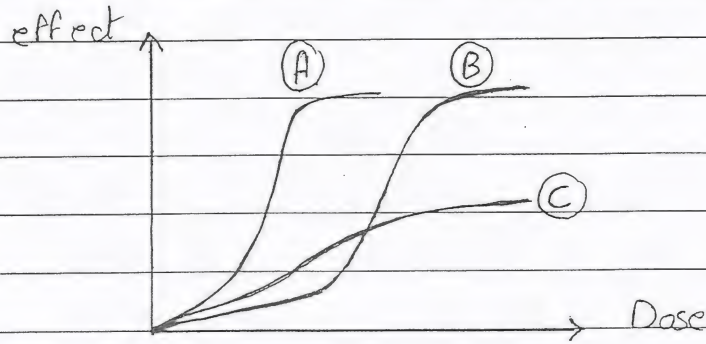
2 substances act to oppose each other's effect

example : NE (norepinephrine) increases heart beats  
while Ach (acetyl choline) decreases heart beats  
 $\therefore$  opposes NE effect

Through Completely different Receptor



A nice graph to understand



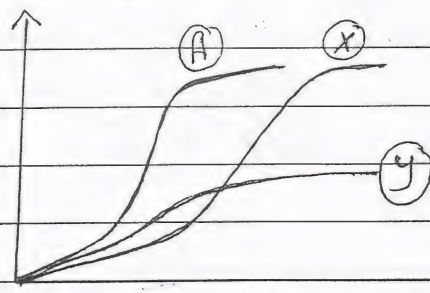
(A), (B) have the same maximum efficacy  
so they are full agonists.

But (A) is more potent than (B) as it give max. effect by lower conc.

(C) doesn't give maximum effect "it's", so it's a partial agonist not a full agonist.

By taking drug (A) only, adding to it a competitive antagonist  $\rightarrow$  it gives us curve (X)

But if we add to it a noncompetitive antagonist it gives us curve (Y)



و قالوا فسرح الحوار  
و فقهه كويس

X  $\rightarrow$  give maximum efficacy As  $\uparrow$  Drug Dose  $\rightarrow$   $\downarrow$  Antagonist  
Leave  $\downarrow$  receptor to Agonist and give  $\downarrow$  Response

Y  $\rightarrow$  not ~ ~ ~ As Drugs bind  $\bar{e}$  all Receptor but its  
ACTs inhibited by  $\downarrow$  Antagonist



في وقتي أنت أخذت drug (A) و competitive antagonist  
 antagonist ده هينافس ال drug على ال receptor سوية  
 لكن مع زيادة ال dose بتأني ال drug ال antagonist  
 سوف يطرده وال drug سوف يعطي ال maximum effect  
 عادي جداً لكن باستخدام Dose أكثر من العادية  
 وهذا هو ما يعبر عنه ال (X) curve

من طبي لو أخذت drug (A) و non competitive antagonist  
 ال antagonist هيتأثر على ال efficacy بتأني ال drug  
 ومهما تزاوا ال dose بتأني ال drug من هيتأثر على  
 ال antagonist ولا على ال efficacy  
 وهذا هو ما يعبر عنه ال (y) curve

كده إحنا خلصنا الجزء ده وفاضل لنا حصة صغيرة  
 أوى من حاجة في الزين

### Drug - interaction

Drug (A) Drug (B)  
 ① Additive effect : 1 + 1 = 2  
 يعني لو أخذت جرعة من (A) و جرعة من (B) ال effect النهائي هيبقى  
 مجموع ال effects بتاعتهم  
 ex Diuretics +  $\beta$  Blocker  $\rightarrow$  hyperTension

② Synergism : 1 + 1 > 2  
 يعني لو أخذت جرعة من (A) و جرعة من (B) هيبقى ال effect النهائي أكثر من  
 مجموع الإثنين على بعض ده يعني بيقتوا بعض

ex  $\text{CCl}_4 + \text{CH}_3\text{OH} \rightarrow \text{Destroy Liver Completely}$   
 Carbon Tetra Chloride ethanol - each one have hepatotoxic effect



③ Potentiation : 0 + 1 > 1  
 يعني drug A ليس له effect لوحده خالص لكن مع وجوده مع يقوى ال effect بتاع (B) ويحصل ال effect بتاعه اكتر من واحد

ex Barbiturates + Analgesic → ↑ Analgesic effect  
 also " not analgesic  
 ومع آخر ما جات

## Drug Safety

### Therapeutic index (TI)

LD50 (Median lethal toxic dose) بين الجرعة التي لها تأثيرات  
التي لا يمكن تحملها  
 ED50 (Median effective dose) ← دosis  
← دوسية زهر

\* To Calculate the therapeutic index :

$$TI = \frac{LD50}{ED50}$$

في انجى دواء (مقياس امان) اللى عنده TI عالية ولا قليلة ؟

• طبعا اللى عنده TI عالية لا تكون دوائه خطيرة ال LD50 الى 10 اضعاف الى  
 دوسية 50% من الناس (مقياس كبيرة) ← Safe

i.e. The Safe drugs are those that have a high therapeutic index

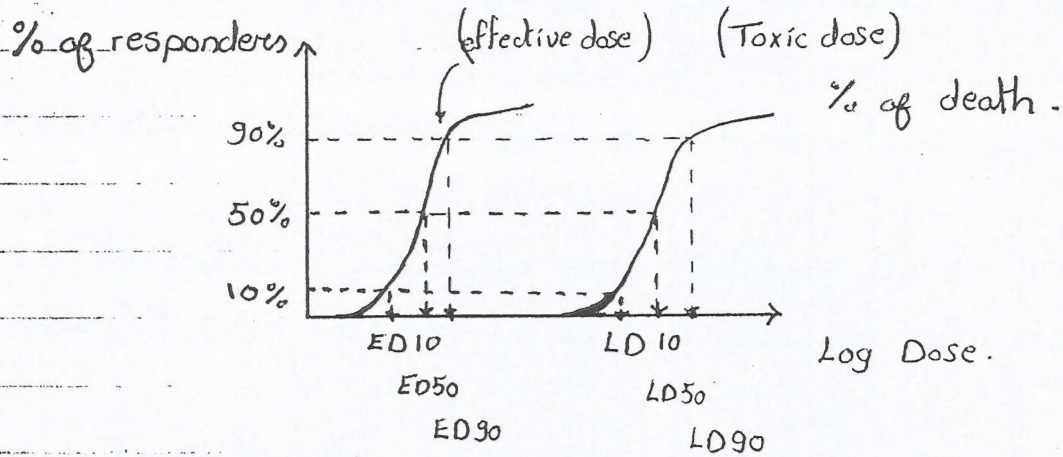
The End

Pray 4 us a lot



هناك Curve في الكتاب ولم يشرح في المحاضرة ولم يقال أصلاً  
 هو مهم له يد له علاته يفهمنا ال Therapeutic index  
 والقانون يتأكد جاء منه اللى هو  

$$TI = \frac{LD_{50}}{ED_{50}}$$



تعالوا نشرح ال curve ده واحدة واحدة علاته نظبطه .

تعالوا ننسب على ال axis بتاع ال Dose وكل شوية نسوق ال effect  
 وقبل كل حاجة ال curve اللى على السفال هو ال % of responders  
 يعنى الناس اللى يتعالج بال dose دى  
 وال curve اللى على اليمين هو ال % of deaths يعنى الناس  
 اللى بتموت من ال dose دى .

ده دلوقتى أنا يا ديت فرضي 100 dose ده صغرة اوى من عشرة منهم  
 فقط استجابوا لا dose دى والباقي جسمهم لم يتأثر نهائى  
 ال dose دى هنسميها [ED10]

ده ابتديت أزود ال dose به خمسين منهم استجابوا والباقي لا  
 ال dose دى هنسميها [ED50] ودى مهمة اوى اوى اوى .



→ بدآت ازود ال dose → تسعیم استجابوا و عسرة لا  
ال Dose دی هتسبعها [ED 90]

→ زودت ال dose → کلهم استجابوا → ED 100

→ زودت ال dose → کله مستجيب و محدش حصله حاجة

→ زودت ال dose → عسرة منهم ماتوا من ال Toxicity  
ال dose دی هتسبعها [LD 10] → ده ال curve ال ایمن

→ زودت ال dose → خمیس منهم ماتوا من ال Toxicity  
ال dose دی هتسبعها [LD 50] مهمة أوی أوی أوی

→ زودت ال dose → تسعیم منهم ماتوا من ال Toxicity  
ال dose دی هتسبعها [LD 90]

① Therapeutic index :  $\frac{LD 50}{ED 50}$  من ال curve ال ایمن  
من ال curve ال ایس

فهمت بٹا یا بٹا القانون جاء منیه ؟  
فهمت ال curve کویس ؟

① TI must be more ①

TI → as it ↑ → as the drug Becomes safer.